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Original Article

# Gender differences in REM sleep behavior disorder: a clinical and polysomnographic study in China

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ABSTRACT

*Objective:* Rapid eye movement (REM) sleep behavior disorder (RBD) has been considered a male-predominant parasomnia, and there is little comparative data on potential differences between males and females. Therefore, the aim of our study was to examine and characterize gender difference in RBD.
*Methods:* Ninety patients diagnosed with RBD were consecutively recruited from a sleep medicine clinic. All patients were assessed by a RBD questionnaire and overnight video polysomnography. Demographic, clinical data, presence of dreams and dream-enacting behaviors, sleep parameters and electromyographic (EMG) activity were compared for male and female patients with RBD.
*Results:* Females were significantly younger than males, both in the mean age of RBD onset (45.3 ± 19.3 vs. 56.2 ± 14.1; $p = 0.027$) and the mean age at diagnosis (50.4 ± 18.2 vs. 61.1 ± 14.1; $p = 0.022$). Secondary RBD was 21% in males and 44% in females ($p = 0.021$). Antidepressant use was more common among females (22%) than males (2%; $p = 0.003$). There was no significant gender difference in dream content (eg, violent and frightening dreams) of RBD patients. However, females had less dream-enacting behaviors, especially in movement related dreams and falling out of bed. Interestingly, no significant difference was found in the quantification of EMG activity during REM sleep between male and female patients.
*Conclusions:* We found significant gender differences in demographics, associated comorbidities, and dream-related behaviors in patients with RBD. Female RBD patients reported significantly less behavior during dreams, but there was no significant gender difference in EMG activity during REM sleep.


## 1. Introduction

Rapid eye movement (REM) sleep behavior disorder (RBD) is a parasomnia characterized by a loss of muscle atonia during REM sleep and dream-enacting motor activity. These abnormal behaviors can cause sleep disruption and injury for the patient or bed partner [1]. Recently, the prevalence of RBD was updated to 2.01% in the elderly population [2]. Previous studies have reported a striking male predominance in typical RBD, with more than 80% of the patients being male [3–7]. Some studies also report that males had more aggressive and violent RBD behaviors than did females [8,9]. However, most existing studies involved small case series or provided very little information about female patients, and gender differences in patients with RBD have not been well characterized. Thus, we performed a study on 90 male and female RBD patients to explore possible gender differences in demographics, RBD symptoms, sleep architecture and REM sleep without atonia (RSWA).

## 2. Methods

### 2.1. Subjects

A consecutive series of 90 patients with a diagnosis of RBD were recruited from the Sleep Medicine Clinic in West China Hospital. RBD was diagnosed based on the criteria of International Classification of Sleep Disorders (edition 2) (ICSD-2) as follows: (1) clinical history of RBD symptoms that are potentially harmful or result in sleep-related injuries to self or sleep partner and/or the presence of abnormal REM sleep behaviors during polysomnography (PSG) monitoring; (2) PSG evidence of REM sleep without atonia (RSWA) including excessive augmentation of submental electromyographic (EMG) tone or excessive submental or limb EMG phasic twitching; and (3) absence of electroencephalography (EEG)

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epileptiform activity during REM sleep [1]. This study was approved by the hospital ethics committee, and all patients gave written informed consent.

Patients were interviewed to obtain demographic information (eg, age and gender) and clinical details including disease duration, associated comorbidities, and the use of medications or substances. Associated neurological disorders were diagnosed according to the common clinical criteria used by consulting neurologists. RBD was classified as secondary or idiopathic. When it was associated with a neurological disorder (eg, narcolepsy, neurodegenerative disease) or medication use (eg, antidepressant), RBD was categorized as secondary. All other cases with absence of any known neurological or clinical disorder were categorized as idiopathic. Patients were defined as early-onset (≤50 y) or late-onset (>50 y) according to the onset age.

### 2.2. Assessment of RBD questionnaire

All patients were assessed for dream contents and dream-enacting behaviors by a 13-item self-reported RBD questionnaire (RBDQ-HK). This questionnaire measures two domains: factor 1 (items 1–5, 13) describes the dream contents and disrupted sleep and factor 2 (items 6–12) assesses the sleep-related behaviors [10]. Each RBD symptom was measured according to the frequency of occurrence of dream and enactment behaviors in a lifetime and on a yearly basis. The maximum score was 5 in each item of factor 1 and 10 in each item of factor 2; thus, the total score was 100 for the questionnaire. The RBD-HK has been demonstrated to be a useful quantitative instrument for clinical symptoms and severity of RBD.

### 2.3. Video-polysomnography (VPSG) and quantification of EMG activity

All patients underwent one overnight VPSG assessment. Recording of the PSG included EEG (F4-M1, C4-M1, O2-M1, F3-M2, C3-M2, O1-M2), bilateral electrooculogram (EOG) (ROC-M1, LOC-M2), submental and bilateral anterior tibialis EMG, electrocardiogram (ECG), nasal-oral airflow, thoracic, and abdominal respiratory efforts, oxygen saturation and body position. Video was recorded simultaneously with the PSG. Sleep stages and associated events were manually scored in 30 s epochs according to the criteria described in the American Academy of Sleep Medicine (AASM) manual [11].

EMG activity during REM sleep was scored manually according to the criteria of the 2007 AASM Manual [11]. Tonic EMG activity was defined as sustained EMG activity more than 50% of the 30-sec epoch with amplitude greater than the minimum amplitude in non-rapid eye movement (NREM) sleep. Phasic EMG activity was scored from a 30-sec epoch of REM sleep in which at least 50% of 3-sec mini-epochs contained bursts of EMG activity lasting for 0.1 to 5.0 sec with amplitudes of four times that of the baseline EMG tone. Quantification of the RSWA was conducted separately in the percentage of 30-sec epochs with tonic and phasic EMG activity. EMG activities associated with respiratory events, periodic leg movements, arousals or signal artifacts were excluded from the analysis.

### 2.4. Statistical analysis

Statistical analysis was performed using SPSS version 17. Descriptive data were presented as mean ± standard deviations or frequencies (percentages). Univariate analysis of categorical data was performed using chi-square or Fisher's exact test as appropriate. Comparison between two groups on continuous data was conducted using Student's t-test or Mann–Whitney U-test. $p < 0.05$ was considered as statistically significant.

**Table 1**
Comparison of clinical variables between males and females with rapid eye movement sleep behavior disorder.

| Clinical features | Male ($n = 63$) | Female ($n = 27$) | $p$ |
|---|---|---|---|
| Age at onset (years) (Mean ± SD) | 56.2 ± 14.1 | 45.3 ± 19.3 | 0.027 |
| Early onset (≤50 years), $n$ (%) | 12 (19%) | 11 (41%) | 0.031 |
| Late onset (>50 years), $n$ (%) | 51 (81%) | 16 (59%) | 0.031 |
| Age at diagnosis (years) (Mean ± SD) | 61.1 ± 14.1 | 50.4 ± 18.2 | 0.022 |
| Idiopathic RBD, $n$ (%) | 50 (79%) | 15 (56%) | 0.021 |
| Secondary RBD, $n$ (%) | 13 (21%) | 12 (44%) | 0.021 |
| Neurodegenerative disease, $n$ (%) | 11 (17%) | 3 (11%) | 0.055 |
| Narcolepsy, $n$ (%) | 1 (2%) | 3 (11%) | 0.079 |
| Antidepressant use, $n$ (%) | 1 (2%) | 6 (22%) | 0.003 |
| RBDQ-HK (Mean ± SD) | | | |
| Factor 1 dreams | 16.9 ± 5.4 | 16.8 ± 5.9 | 0.884 |
| Factor 2 behaviors | 38.2 ± 10.8 | 31.6 ± 10.2 | 0.019 |
| Total score | 55.0 ± 12.4 | 48.4 ± 12.1 | 0.098 |

RBD, rapid eye movement (REM) sleep behavior disorder; RBDQ-HK, REM sleep behavior disorder questionnaire-Hong Kong.

## 3. Results

Of the 90 patients with RBD, 63 (70%) were male and 27 (30%) were female. Demographic and clinical data were analyzed according to gender. Table 1 presents the characteristics of age, comorbidity, dreams, and enacting behaviors of male and female patients with RBD. There was a significant gender difference regarding age of onset (56.2 ± 14.1 vs. 45.3 ± 19.3, $p = 0.027$) and diagnosis (61.1 ± 14.1 vs.50.4 ± 18.2, $p = 0.022$). Females had a higher proportion of early-onset RBD than did males. Idiopathic RBD (IRBD) was found in 79% (50/63) of the males and 56% (15/27) of the females; the difference was significant ($p = 0.021$). RBD in males tended to be associated with neurodegenerative diseases, including Parkinson's disease (PD), dementia with Lewy bodies (DLB), and multiple system atrophy (MSA) (17% vs. 11%, $p = 0.055$). Of the patients with neurodegenerative diseases, 11 were males (9 PD, 1 DLB and 1 MSA) and three were females (2 PD and 1 MSA). The secondary form of RBD was associated with narcolepsy in 2% of males and 11% of females ($p = 0.079$). Antidepressant use resulted in RBD in more females compared to males (22% vs. 2%, $p = 0.003$).

The males had significantly higher scores for behavioral manifestations (factor 2) ($p = 0.019$), whereas the mean score of dream contents (factor 1) showed no significant gender difference ($p = 0.884$). A more detailed analysis in the 13 items of the RBD questionnaire, using scoring in two profiles, showed significant gender differences (Fig. 1). Males had significantly more dream-related movements and more falling out of bed during sleep. However, there were no significant differences in amounts of vivid, violent, and frightening dreams between the two groups. Reported incidences of disturbed sleep was similar for male and female patients with RBD (2.1 ± 2.1 vs. 2.2 ± 2.2, $p = 0.914$).

Comparisons of PSG parameters for male and female RBD patients are presented in Table 2. Females had a significantly higher percentage of slow wave sleep ($p = 0.032$) than did males. In contrast, males spent more time in stage 1 sleep than did females ($p = 0.028$). Other sleep stages, sleep latency, total sleep time, and sleep efficiency in sleep architecture did not show statistical differences between males and females. Likewise, apnea-hypopnea index (AHI) and periodic limb movement index (PLMI) did not show significant gender differences. Interestingly, behaviors during sleep were fewer in females, but no gender differences were found in the percentages of either tonic or phasic EMG activities ($p > 0.05$).

## 4. Discussion

The present study is consistent with previous reports showing a male predominance (70%) for RBD. We found clear differences in

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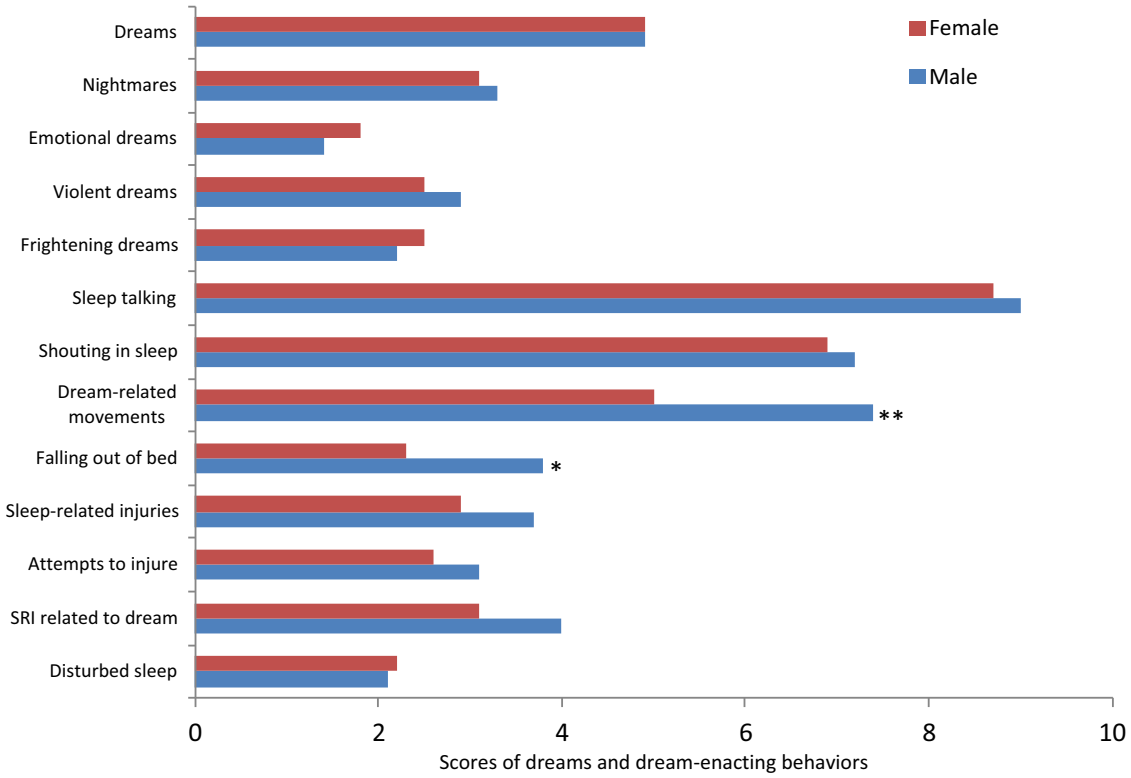


**Fig. 1.** Gender difference in scoring profiles of the REM sleep behavior disorder questionnaire. SRI, sleep-related injuries. *p < 0.05; ** p = 0.001.

demographics, clinical presentation and PSG findings in males and females with RBD. The mean age of RBD onset (45 years) and diagnosis (51 years) was younger in females, indicating that females have a higher proportion of early-onset RBD than do males. This result is in line with previous studies that found a greater proportion of females in a group of early-onset RBD patients compared to a late-onset group [12–14] and with a review of 126 studies that reported the mean age of onset and diagnosis in women with RBD was 48 years and 54 years, respectively [8]. The younger age of females might be due to secondary factors such as narcolepsy and antidepressants use. Narcolepsy has been proposed to be the etiology in the first decade of life in female RBD [8].

RBD is frequently associated with neurodegenerative diseases, in particular the synucleinopathies such as PD, DLB and MSA [6].

**Table 2**
Comparison of sleep architecture and electromyographical activity variables between males and females with rapid eye movement sleep behavior disorder.

| Sleep variables | Male ($n = 63$) | Female ($n = 27$) | $p$ |
|---|---|---|---|
| Sleep latency (min ± SD) | 23.5 ± 24.6 | 15.9 ± 20.2 | 0.157 |
| REM sleep latency (min ± SD) | 127.1 ± 74.7 | 172.4 ± 125.9 | 0.249 |
| Sleep efficiency (% ± SD) | 77.6 ± 12.6 | 80.7 ± 15.5 | 0.223 |
| Total sleep time (min ± SD) | 384.0 ± 83.7 | 396.0 ± 82.4 | 0.498 |
| Stage 1 (% ± SD) | 19.9 ± 13.1 | 12.1 ± 10.8 | 0.028 |
| Stage 2 (% ± SD) | 51.4 ± 17.6 | 55.8 ± 12.7 | 0.277 |
| Stage 3 (% ± SD) | 9.3 ± 7.9 | 13.1 ± 6.0 | 0.032 |
| Stage REM sleep (% ± SD) | 19.4 ± 9.6 | 19.0 ± 8.4 | 0.833 |
| WASO (min ± SD) | 122.1 ± 70.9 | 120.7 ± 111.8 | 0.466 |
| AHI | 6.4 ± 9.1 | 2.7 ± 3.1 | 0.126 |
| PLMI | 15.3 ± 16.9 | 13.8 ± 16.8 | 0.715 |
| REM sleep periods, ($n$) | 5.4 ± 2.9 | 4.9 ± 2.8 | 0.546 |
| Phasic EMG activity (% ± SD) | 9.4 ± 8.4 | 9.4 ± 12.4 | 0.466 |
| Tonic EMG activity (% ± SD) | 20.1 ± 16.5 | 21.5 ± 18.4 | 0.988 |
| Phasic + Tonic EMG activity (% ± SD) | 29.4 ± 18.1 | 31.2 ± 23.2 | 0.907 |

AHI, apnea-hypopnea index; EMG, electromyography; PLMI, periodic limb movement index; REM, rapid eye movement; WASO, wake after sleep onset.

In our study, referral bias is a plausible explanation for the smaller proportion of RBD associated with neurodegenerative disease (16%). However, this result that only 11% of female cases had neurodegenerative disease corresponds with 10% of females reported in a previous study [13]. Ju et al. found neurodegenerative disease was frequently coincident with RBD in older men [13], eg, PD has a ratio of approximately 2:1 for men compared to women [15]. Therefore, the male predominance of RBD was considered to reflect underlying neurodegeneration [2]. In our study, this suggestion is supported by the trend for more neurodegenerative disorders in males compared to females ($p = 0.055$). Narcolepsy is commonly comorbid with RBD, but the frequency of RBD has not been found to vary with gender with comorbid narcolepsy [16]. The ratio of females with narcolepsy (11%) we found was similar to that reported in other studies (10% or 11%) [8,13]. Antidepressants have a strong association with RBD, and we found a higher prevalence of antidepressant use in female patients in this study (22%:2%). In published work, up to 46.1% of RBD patients use antidepressants, and it is especially common (52.5%) in female patients [13]. The increased proportion of women with antidepressant use [14] could be due to the increased prevalence of depression in women [17]. A majority of studies suggest antidepressants (eg, tricyclic antidepressants and selective serotonin reuptake inhibitors) may induce RBD [13,18]; however, Wing et al. speculated that antidepressants might be a precipitating agent instead of having a causal role in RBD in psychiatric patients [19,20]. In total, 56% of female patients were idiopathic for RBD in our study. Ju et al. reported a higher proportion of idiopathic RBD in females (70%), that because of use of antidepressants or other medications were not deemed due to secondary factors [13].

The frequency of dreams and vivid dream content (emotional, violent and frightening imagery) were the same in male and female RBD patients. This finding of no significant gender differences in dream content is consistent with the literature [5,21]. In contrast

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to males with RBD, females were not observed less violent dream content. Interestingly, we found that female patients showed significantly less dream-enacting behaviors during sleep, especially in movement related dreams and falling out of bed. Similarly, several previous studies have shown that males with RBD have more violent and aggressive dream enactment [8,9,22]. Bjornara et al. suggested that this difference might arise from biological differences and the fact that males usually show more aggressive behavior than females in most mammalian species [9]. However, Wing et al. found no differences in behavioral symptoms during sleep between male and female patients [5]. Small sample sizes and variation in assessment of questionnaire might also contribute to these inconsistent results.

There are several possible explanations for the male predominance of RBD. First, the sex hormone has been hypothesized to play a role in male predominance and more violent behaviors during sleep [23]. However, a study examining serum sex hormone levels of RBD male patients found no difference compared with the controls [24]. This result suggests that androgenic abnormalities might not account for male predominance [24]. Another studies pointed toward a neuroprotective effect of estrogen against dopamine neurodegeneration in the nigrostriatal regions; this hormone in females may be a protective agent from developing of RBD [24]. Unfortunately, there is no consensus on this possibility across studies [25]. Second, males with more violent and disruptive behaviors may be prone to seek medical consultation [23,26]. Third, neurodegenerative disease associated with RBD itself is predominant in males. Previous reports and our results support this finding. Lastly, women may be underestimated in the RBD population due to the use of questionnaires that are inadequate for detecting behaviors during sleep in females [8]. Additionally, women typically live longer than men, and because of this, they may be more likely to sleep alone and may be unaware of their abnormal nightly behaviors.

Our data showed no clear gender difference for either the percentages of tonic or phasic EMG activities during REM sleep. To our knowledge, this is the first study to quantify EMG activity in males and females with RBD. Previous studies only compared dream- and dream-enacting behavior using a RBD questionnaire, but did not quantify RSWA. Although more motor activities (eg, limb movements and falling out of bed) were observed in male RBD patients, the chin EMG tone on the examination night was not correlated with the score of behavioral activity during sleep. One possible explanation is that we only performed a quantitative EMG analysis for the mentalis muscle. Frauscher et al. reported that EMG activity was only present in 35% of behaviors when using the mentalis muscle alone, whereas using a combination of muscles, EMG activity was present in 95% of all motor and vocal manifestations [27].

In sleep architecture, female patients with RBD spent significantly more time in slow wave sleep than did males. Similarly, Silva et al. examined the effect of gender on the sleep pattern of patients with sleep disorders and found that women had more deep sleep than did men [28]. Furthermore, our results are consistent with previous laboratory-based normative sleep values in male and female adults [29]. Gender differences in sleep could be due the effects of female hormones on sleep architecture [28,30]. In addition, slow wave sleep decreases with age, and younger ages could be a possible reason for the longer deep sleep in female RBD patients.

Unfortunately, a limitation of this study is that we did not exclude the potential effects of secondary factors (e.g. comorbidities and drug usage). Although effects of these factors appeared to be small when we did an analysis (data not shown) of IRBD, future studies conducted on IRBD with greater sample sizes could facilitate comparisons of gender differences across subtypes of RBD.

## 5. Conclusion

The current study describes the clinical and PSG findings of females and males with RBD. We found that females with RBD were younger, had more antidepressant use and exhibited less dream-related behaviors than male. However, the quantification of EMG activity did not show significant differences between males and females. There also were specific gender differences in sleep patterns in that females had more slow wave sleep and less stage 1 time. We suggest that it is important to recognize gender differences in RBD as this may enable clinicians to understand the underestimation of RBD in female patients and also more accurately diagnose RBD in both sexes.

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## Conflict of interest

The authors have indicated no financial conflicts of interest in this article.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.10.020.

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